"preventing" is actually redundant, and the scope is unaffected. On page 10 of the Office Action, the Examiner makes the finding that both preventing and treating were well known in the prior art, but finds that Applicants had not provided any guidance or working examples, and, therefore, the application was nonenabling. In response, Applicants submit that the Examiner's inconsistent position is also inconsistent with the law. The specification need not provide guidance or working examples for embodiments that are well known in the prior art. See, for example, *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986), for the propositions that 1) "a patent need *not* teach, *and preferably omits,* what is well known in the art (emphasis added)," and 2) lack of enablement rejections and prior art rejections must be internally consistent.

With respect to claim 25, contrary to the Examiner's statement in line 2 on page 3 of the Office Action, Applicants point out that this claim does not recite "preventing," so claims 25-29 should not have been included in the rejection anyway.

Claims 32-33 were rejected under 35 USC § 102(b) as being anticipated by Suzuki et al. ("Suzuki"), U.S. Patent No. 5,145,781, or Frazier, U.S. Patent No. 4,297,348. In response, Applicants point out that claims 32-33 do not recite alpha-glucosylrutin, and, therefore, Suzuki does not read on the instant claims. With respect to Frazier, claims 32-33 no longer recite naringin.

Claims 32-33 were rejected under 35 USC § 102(b) as being anticipated by Yoneyama et al., U.S. Patent No. 5,565,435. In response, Applicants point out that claims 32-33 refer to "alpha-glucosylquercitrin," not "alpha-glucosylquercetin." The Examiner has not shown these compounds to be identical, and the undersigned is unaware of such identity.

Claims 30-33 were rejected under 35 USC § 102(e) as being anticipated by Whittle, U.S. Patent No. 5,466,452. In response, Applicants point out that claims 30-33 require specific flavonoids and the Examiner has not identified any from the list as being contained in Whittle's formulations. In the absence of such identification, the Examiner cannot have made out a *prima facie* case of anticipation. In response, Applicants would remind the Examiner that anticipation requires that each and every element as set forth in the claim must be found, either expressly or inherently described, in a single prior art reference, and, further, that the absence in the prior art reference of even a single claim element precludes a finding of anticipation. *In re Robertson,* 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Unless the Examiner can show in the reference the particular flavonoids required by the instant claims, an essential claim element is altogether missing from the reference and, thus, there cannot be anticipation.

Claims 25-33 were rejected under 35 USC § 102(e) as being anticipated by N'Guyen et al. ("N'Guyen"), U.S. Patent No. 5,431,912. In response, Applicants again point out that the rejected claims require specific flavonoids and the Examiner has not identified any from the list as being contained in N'Guyen's formulations. Again, in the absence of identification in the

reference of any of the particular flavonoids required by the instant claims, the Examiner cannot have made out a *prima facie* case of anticipation.

Claims 19-29 were rejected under 35 USC § 103(a) as being obvious over N'Guyen et al. ("N'Guyen II"), U.S. Patent No. 5,587,171, in view of Middleton et al. ("Middleton"), *The Flavonoids, Advances in Research Since 1986,* and Harrison's, *Harrison's Principles of Internal Medicine.* In response, Applicants submit that the cited combination of references does not make out a *prima facie* case of obviousness. The Examiner concedes that the primary reference, N'Guyen, does not teach the topical application of flavonoids for treating immunosuppression caused by UVB. Accordingly, that suggestion, and the suggestion that topical application can successfully protect cells that participate in the immune response of skin from the damaging effects of UVB (claims 25-29) must come from the secondary references. These secondary references deal mainly with the *internal effects* of flavonoids, and do not provide any reasonable expectation that either specific flavonoids or flavonoids as a class would be successful in treating immunosuppression caused by UVB or in protecting cells that participate in the immune response of skin from the damaging effects of UVB. Consequently, the cited combination of references does not, in fact, make out a *prima facie* case of obviousness.

In the second paragraph on page 8 of the Office Action, the Examiner explains his reliance on Middleton. The only mention of successful topical application is the reference to topical application of quercetin in the next to last sentence of the paragraph, which is said to be

supported by the 3rd to 8th paragraphs of Middleton on page 642. Those paragraphs, contrary to the Examiner's reading, deal mostly with *oral application* of flavonoids, thus the various references throughout to "feeding," *"in vivo,"* "[D]ietary," "diet," etc.

There is mention in the 3rd paragraph on the page that topical application of quercetin protected mice against certain chemical-induced skin tumorigenesis. There is also mention in the 8th paragraph that topical application of quercetin and myricetin inhibited PAH metabolism and PAH-DNA adduct formation, "thus indicating a *possible* mechanism of chemoprevention of skin cancer by flavonoids." Other than that, Applicants have been unable to find any mention of topical application of flavonoids in the quoted paragraphs.

Applicants submit that these two passages are manifestly inadequate to suggest the topical application of flavonoids to skin for the purposes of treating immunosuppression caused by UVB or in protecting cells that participate in the immune response of skin from the damaging effects of UVB, nor does Middleton reveal a reasonable expectation that the specific flavonoids mentioned or flavonoids as a class would be successful in this endeavor. Indeed, there is no mention of UVB at all, and the only conclusions were of "possible" flavonoid mechanisms of action.

Harrison's is relied upon "to show the general knowledge in the art about the etiology of solar radiation and systemic immune response caused by UV-B exposure." However, such

knowledge combined with Middleton's unclear teachings does not bridge any of the gaps in Middleton's teachings as discussed above. The combination of N'Guyen, Middleton and Harrison's does not suggest the topical application of flavonoids to skin for the purposes of treating immunosuppression caused by UVB or in protecting cells that participate in the immune response of skin from the damaging effects of UVB, nor does the combination reveal a reasonable expectation that the specific flavonoids mentioned or flavonoids as a class would be successful in this endeavor.

In short, Applicants submit that the cited combination of references fails to make out a *prima facie* case of obviousness. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

Claims 19-33 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 4 of U.S. Patent No. 5,952,373 and claims 1-5 of U.S. Patent No. 6,121,243.

Claims 19-33 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the pending claims of USSN 09/656,598 and 09/540,007.

In response to both obviousness-type double patenting rejections, Applicants respectfully request that these issues be held in abeyance until allowable subject matter is indicated, at which time Applicants will either prove patentable distinctness or take other appropriate action, for example, file a suitable terminal disclaimer.

Applicants believe that the foregoing constitutes a bona fide response to all outstanding objections and rejections.

Applicants also believe that this application is in condition for immediate allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,
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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that the foregoing Amendment Under 27 CFR §1.111, the attached Mark-Up Showing the Changes Made in the Previous Claim to Yield the Claim as Amended Above, and Petition for Extension of Time (14 pages total) are being facsimile transmitted to the United States Patent and Trademark Office on the date indicated below.

Date: November 22, 2002

By _____
Kurt G. Briscoe

MARK-UP SHOWING THE CHANGES MADE IN THE PREVIOUS CLAIM TO YIELD THE CLAIM AS AMENDED ABOVE

--19. A method for [preventing or] treating immunosuppression of skin cells induced by UVB radiation, said method comprising topically applying to the skin of a person in need thereof an effective amount therefor of a cosmetic or dermatological formulation comprising:

a) one or more flavonoids selected from the group consisting of alpha-glucosylrutin, alpha-glucosylmyrictrin, alpha-glucosylisoquercitrinin, alpha-glucosylquercitrin, quercitin, rutin, chrysin, kaempferol, myricetin, rhamnetin, apigenin, luteolin, naringin, hesperidin, naringenin, hesperitin, morin, phloridzin, diosmin, fisetin, vitexin, neohesperidin dihydrochalcone, flavone, glucosylrutin and genistein;

b) optionally one or more cinnamic acid derivatives; and

c) optionally an antioxidant;

and preventing or treating immunosuppression of skin cells induced by UVB radiation. --

--32. A cosmetic or dermatological formulation comprising:

a) one or more flavonoids selected from the group consisting of alpha-glucosylmyrictrin, alpha-glucosylisoquercitrinin,

alpha-glucosylquercitrin, myricetin, rhamnetin, apigenin, [naringin,] hesperidin, hesperitin, morin, phloridzin, diosmin, vitexin, neohesperidin dihydrochalcone, flavone, glucosylrutin and genistein;

b) optionally one or more cinnamic acid derivatives; and

c) optionally an antioxidant. - -